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Questions and answers on Didanosine and associated names (didanosine, gastro-resistant capsules, 200, 250 and 400 mg)

Outcome of a procedure under Article 29(4) of Directive 2001/83/EC

On 19 September 2013, the European Medicines Agency completed an arbitration procedure following a disagreement among Member States of the European Union (EU) regarding the authorisation of the medicine Didanosine. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of Didanosine outweigh its risks, and the marketing authorisation can be granted in the United Kingdom and in the following Member States of the EU: France, Germany, Italy, the Netherlands, Portugal, Romania and Spain.

What is Didanosine?

Didanosine is an antiviral medicine used in combination with other medicines to treat patients infected with human immunodeficiency virus type 1 (HIV-1), a virus that causes acquired immune deficiency syndrome (AIDS).

Didanosine belongs to a class of medicines called nucleoside analogues or nucleoside reverse-transcriptase inhibitors (NRTIs). It blocks the activity of reverse transcriptase, an enzyme produced by HIV-1 that allows it to make more viruses in the cells it has infected. By blocking this enzyme, didanosine, taken in combination with other antiviral medicines, reduces the amount of HIV in the blood and keeps it at a low level. Didanosine does not cure HIV infection or AIDS, but it may delay the damage to the immune system and the development of infections and diseases associated with AIDS.

Didanosine is a hybrid medicine which means that it is similar to a 'reference medicine' already authorised in the EU called Videx EC. It is available as gastroresistant tablets. 'Gastroresistant' means that the tablet's contents pass through the stomach without being broken down until they reach the intestine. This prevents the active substance from being destroyed by the acid in the stomach.

Why was Didanosine reviewed?

Aurobindo Pharma (Malta) Limited submitted Didanosine to the UK medicines regulatory agency for a decentralised procedure. This is a procedure where one Member State (the 'reference Member State', in this instance the United Kingdom) assesses a medicine with a view to granting a marketing

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authorisation that will be valid in this country as well as in other Member States (the 'concerned Member States', in this instance France, Germany, Italy, Netherlands, Portugal, Romania and Spain).

However, the Member States were not able to reach an agreement and the UK medicines regulatory agency referred the matter to the CHMP for arbitration on 4 March 2013.

The grounds for the referral were objections raised by France and the Netherlands that the bioequivalence study carried out under fed conditions did not show that Didanosine was bioequivalent to its reference medicine, Videx EC. Although the presence of food in the stomach lowers the amount of active substance that can be absorbed and these medicines should therefore be taken on an empty stomach, as Didanosine is a gastro-resistant preparation bioequivalence in fed conditions must be shown to grant the marketing authorisation. Two medicines are bioequivalent if they produce the same levels of the active substance in the body.

What are the conclusions of the CHMP?

Based on evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that bioequivalence to the reference medicine has been shown when taken on an empty stomach, and under fed conditions when considering the overall exposure to the active substance (a measure known as AUC). Although the Committee noted that the maximum concentrations of active substance in the blood when taken with food were somewhat higher after Didanosine than after the reference medicine, it considered that the difference was not clinically relevant since the medicine should be taken on an empty stomach, which produces much higher concentrations, and these small variations in the concentration of the active substance in the blood would therefore not increase the risks. The CHMP therefore concluded that the benefits of Didanosine outweigh its risks and recommended that the marketing authorisation be granted in the concerned Member States.

The European Commission issued a decision on 20 November 2013.